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REMARKS/ARGUMENTS

Claims 29-128 are pending. Favorable reconsideration is respectfully requested.

Applicants would like to thank Examiner Collins for the helpful and courteous discussion held on June 1, 2004. During that discussion, amendments to over come the rejections based on the cited rejections were discussed. The rejections under 35 U.S.C. §112, first paragraph, were also discussed. The following remarks expand on the discussion with the Examiner.

The present invention relates to an isolated DNA sequence encoding a protein, wherein the protein is capable of modulating DNA replication in plant cells and comprises SEQ ID NO: 6 or an amino acid sequence having more than 50% sequence identity to SEQ ID NO: 6. See Claim 29. The present invention also relates to methods of using this DNA sequence (see Claims 49-83) and plant cells and plants obtained thereby (see Claims 84-128).

The rejection of Claims 10-11 and 14-15 under 35 U.S.C. §102(b) over Rounsley et al. is respectfully traversed. The reference fails to describe the claimed DNA sequence.

Rounsley et al. describe a nucleic acid sequence from the Genome Survey Sequence (GSS) database. This is a database of single run short sequencing data, the quality of which is often very poor. Applicants submit that (1) the sequence described by Rounsley et al. does not encode a protein at all and (2) that even a theoretical translation is the sequence described by Rounsley et al. is not capable of modulating DNA replication.

The sequence described by Rounsley et al. is not suitable for encoding a protein because it contains too many stop codons. See Figure 1 attached hereto. In addition, even if one would have tried to translate the sequence described by the reference into a protein using a translation program, one would have ended up with 6 possible amino acid sequences as shown in Figure 1 attached hereto.

Furthermore, one would not have been capable of determining which one of the 6 possible translations could be a protein capable of modulating DNA replication in plant cells because there are too many stop codons to believe that any of the translations is a protein capable of modulating DNA replication in plant cells. In addition, most likely one would choose translation No. 5 because that translation has the lowest number of stop codons. Therefore, Applicants submit that one was even dissuaded from deducing and recognizing that the DNA sequence described by Rounsley et al. encodes a protein comprising SEQ ID NO: 6.

Based on the foregoing, Rounsley et al. fail to disclose the claimed DNA sequence and methods of use. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 10-11 and 24-28 under 35 U.S.C. §102(b) over Hemerly et al. is respectfully traversed. The reference fails to describe the claimed DNA sequence and methods of use.

As suggested by the Examiner, the claims have been amended to recite an isolated DNA sequence. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §101 is believed to be obviated by the amendment submitted above.

As suggested by the Examiner, the claims have been amended to recite an isolated DNA sequence. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §112, first paragraph, for an alleged lack of written description, is respectfully traversed.

There are at least three examples of sequences which fall within the scope of Claim 29 described in the present specification. Those sequences are SEQ ID NO: 6 (which encodes cdc27A1 protein), SEQ ID NO: 14 (which encodes cdc27A2 protein), and SEQ ID NO: 15 (which encodes cdc27B protein). As can be seen in the alignment presented in Figure 6 of the present application, the proteins encoded by those sequences comprise SEQ ID NO: 6 or a peptide having at least 50% amino acid identity with SEQ ID NO: 6. Thus, the specification of the present application describes multiple species within the genus embraced by Claim 29. In addition, there is an implicit disclosure of more sequences because, based on the knowledge of explicitly described cdc27 sequences, one could isolate equivalent genes from other plant species using routine experimentation. It was known at the time the present application was filed that those equivalent genes may have some sequence variation. It would be recognized that isolation of such equivalent genes from other plant species is routine once the sequence of the Arabidopsis genes are known, i.e., based on the sequences described in the present application one can readily isolate the orthologue from another plant species.

In view of the foregoing, the present application satisfies the written description requirement of 35 U.S.C. §112, first paragraph. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §112, first paragraph, for an alleged lack of enablement, is respectfully traversed. The present specification provides a detailed description of how to make and use the DNA sequence recited in Claim 29 so that the scope of the invention can be practiced without undue experimentation.

Applicants submit that as described in the present specification from page 16, line 32 to page 21, line 15, the claimed nucleic acids are isolatable from genomic libraries by routine methods. Based on the sequences of the present invention was possible to isolate a true cdc27 protein, without undue experimentation for the skilled person, because this isolation can be done by routing experiments like hybridization or PCR.

The Examiner states that cdc27 proteins have 16 different exons. The Examiner raised the concern that the effect of a peptide having only 1 exon (SEQ ID NO 6) is unpredictable. To meet the Examiner's concern, Claim 29 specifies that the protein comprises SEQ ID NO: 6 and is capable of modulating DNA replication in plant cells. That recitation is supported by the specification at page 6, lines 23-25, which states that the presence of exon SEQ ID NO: 6 is responsible for promoting APC-substrate action and DNA-replication. It is further supported by the common knowledge that the N-terminus of cdc27 proteins harbors the highly conserved in CDC27/NUC2-LIKE domain (see description at page 7 of WO 01/02430, lines 36-37). SEQ ID NO 6: (VNLQLLARCYLSNSQAYSAYY ILKGSK) is a large portion of this conserved domain. Therefore, it is submitted that the effect of the presence of SEQ ID NO: 6 is a functional effect of the protein, which functional effect is to the promote APC substrate action and therewith DNA-replication.

With respect to "undue experimentation," the specification of the present application provides guidance to use proteins comprising SEQ ID NO 6, which is part of a stretch of at least 161 amino acids, which is part of a cdc27 domain and which is part of a protein with the biological function of modulating DNA replication. No undue experimentation is necessary

since the presence of SEQ ID NO: 6 is related to the biological function of the protein as it contributes to APC substrate activity and therewith in DNA replication.

The Examples of the present application also provide explicit teaching for making and using the claimed DNA sequence.

Example 2 describes the isolation of the cdc27A1 gene, which is an example of a sequence which comprises SEQ ID NO: 6 and is capable of modulating DNA replication in plant cells.

Example 4 describes mutant cdc27 proteins. The muteins described in are related to SEQ ID NO: 6 as follows:

- Loss of function created by insertion of proline in SEQ ID NO: 7 (this mutein still comprises SEQ ID NO: 6).
- Creation of a mutant with a N-terminal deletion of at least 100 bp: this mutant does not comprise SEQ ID NO: 6 anymore and is therefore useful for understanding the contribution of the presence of SEQ ID NO: 6 to the biological function.
- This third type of muteins contain SEQ ID NO: 6.
- The fourth type of muteins is also encompassed within the scope of the invention as they may comprise SEQ ID NO: 6.

Example 5 relates cdc7, and is relevant for the description of the cloning steps and vectors, which are referred to in the Examples which relate to SEQ ID NO: 6.

Example 6 is a prophetic example of how to obtain male sterility in plants using a cdc27 protein which is mutant and which is cloned under control of a tapetum specific example and therefore disrupts cell division.

Example 7 is a hypothetical example which describes that the cdc27 muteins can be used to increase endoreduplication as mentioned in Example 4. Example 7 provides additional details on how to clone the mutants and to transform them into plants.

Example 8 describes a study of the natural expression occurrence of the cdc27 protein, which comprises SEQ ID NO: 6.

Example 9 describes cloning a gene encoding a cdc27B protein, which comprises SEQ ID NO: 6.

Example 10 describes the cloning of cdc27B protein, which comprises a peptide that is at least 50% identical to SEQ ID NO: 6.

In addition, Applicants have also conducted the experiments described below.

Transformation of Tobacco with cdc27A1

Tobacco plants were transformed with a 35S::Atcdc27A1 construct. These plants showed improved characteristics (or improved or useful phenotypes) such as improved growth characteristics, which is manifested by improved yield, improved plant height and improved biomass. See Figure 2 attached hereto. In addition, more cell division, which is manifested by more branching was also observed (see Figure 2). The plants transformed plants also had more leaves as shown in Figure 3 attached hereto and bigger leaves as shown in Figure 4 attached hereto.

Transformation of Arabidopsis with cdc27B

Arabidopsis plants were transformed with a 35S::Atcdc27B construct and the resulting plants showed improved characteristics (or improved or useful phenotypes) such as improved growth characteristics manifested by stay-green phenotype. See Figure 5 attached hereto. Figure 5 also shows that the transformed cells had more cell division as manifested by more branching and more leaves.

In view of the foregoing, the claims of the present application satisfy the criteria for enablement set forth in MPEP §2164 as discussed below.

(A) The Breadth of the Claims.

The claims specify proteins which have to meet the following requirements.

(1) Structurally, they must comprise SEQ ID NO: 6 or an amino acid sequence having more than 50% sequence identity to SEQ ID NO: 6.

(2) Functionally, they must be capable of modulating DNA replication in plant cells.

(B) The Nature of the Invention.

The present invention constitutes the first identification of a new class of proteins in plants and constitutes the first disclosure of methods to improve plant growth characteristics based on these proteins. The methods of the invention and there broad applicability are illustrated by the experimental data described above.

(C) The Level of One of Ordinary Skill.

At the time the present application was filed, the skilled person was aware how to determine whether a protein was capable of modulating DNA replication by checking the DNA level of the cells and/or the effect on cell division, for example, as described in the specification of the present application.

(D) The Amount of Direction Provided by the Inventor.

A sufficient number of DNA species and structural features are given. Sufficient guidance for making construct and transgenic plants are given, as well as the phenotype of such plants, is provided by the specification of the present application.

(G) The Existence of Working Examples.

The prophetic working in the specification as filed, are supplemented by the experimental data discussed above.

(H) The Quantity of Experimentation Needed to Make or Use the Invention Based on the Content of the Disclosure.

One would just have to clone a cdc27 protein and transform it into a plant to see the effect on cell division and/or DNA replication.

Based on the foregoing, the claims are enabled. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §112, second paragraph, is believed to be obviated by the amendments submitted above.

The objection to the claims is believed to be obviated by the amendment submitted above. Accordingly, withdrawal of those objections is respectfully requested.

Regarding the Restriction Requirement, Claims 29-48 are directed to the elected DNA sequences. Claims 49-83 are directed to methods which recite the same DNA sequences as specified in Claims 29-48. Claims 84-128 are directed to plant materials obtained by the claimed methods. Since Claims 29-48 are allowable as discussed above, Claims 49-128 should be rejoined under the provisions of MPEP §821.04.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon

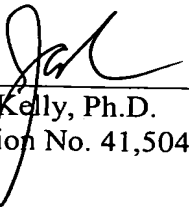

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Figure 1: *The 6 possible translations of GSS Rounsly et al. are full of stopcodons and therefore, the GSS does not encode a protein. Furthermore, none of the 6 possible translations has a startcodon.*

>_1
C*NLG*YSFNSS*ESIHSFSLWSGIFSTFVVVVQFLASVSRNHVNK*LAFLFDHFLNFPLI*VNLQLLATSY
LQNNQAYSAYHLLKGAWHCFLTCCLLAF*SEFCTFFC*VVLIIFVYIFFFCYVKEHKWLSPDTCSHYHAS
RWTFSMKLNLHSALLMNLVRRYLMFSGILPLFAY*MSFYKNSVSVSGPYLLI*FSEDNNMLLIIVX
>_2
VKIWVNTASIVVEKVFIHSAFGLEYFQHS*WLSSF*LQLVEIMSINDWPFCLITF*IFLLYRLICSY*PPATC
RIIKLTVHIIC*RVRGIVS*LVAC*PFSQNFAPSFVRSF*LSLYIYFFFVM*RNTNGSVPILVRIIMLPDGPSQ*
S*ICTLPC**TWCGGI*CSLVFCLYSLTECHF
TKTVCQFLDLIY*FSSVKITTCF*LLC
>_3
LKFGLIQLQ**LRKYSFIQPLVWNIFNIRSGCPVSSFS**KSCQ*MIGLFV*SLSEFSSYIG*FAAISHQLPAE
*SSLQCISSAKGCVALFLDLLLVSLLVRILHLLLLGRFDYLCIYIFFLLCKGTQMAQSRYLFALSCFQMDLL
NEAESALCPVNEPGAEVFNVLWYFAFIRLLNVIL
QKQCVSFWTLFIDLVQ*R*QHASDYC
>_4
HNNQKHVVIFTELNQ*IRSRN*HTVFVK*HSVSE*RQNTREH*IPPHQVH*QGRVQIQLH*EGPSGSMIM
RTSIGTEPFVFLYITKKKYIYKDNQNDLTKEGAKF*LKG*QATSQETMPRTL*QMICTVSLIILQVAGG**L
QINLYKRKIQKVIKQKGQSFIDMISTN*S*KLDNHYEC
*KYSRPKAE*MNTFSTTIEAVLTQILT
>_5
AQ*SEACCYLH*TKSINKVQKLTHCFCKMTFSKRIKAKYQRTLNTSAPGSLTGQSADSASLRRSIWKHD
NANKYRD*AICVPLHNKKKIYIQR*SKRPNKRRCKILTKRLTSNKSRNNATHPLADDMHCKLDYSAGSW
WLIAAN*PI*EENSESDQTKRPIIY*HDFY*LKLETGQPLRMLKIFQTKG*MNEYFLNYY*SCINPNFNX
>_6
TIIRSMLLSSLN*INK*GPETDTLFL*NDIQ*ANKGKIPENIKYLRTRFINRAECRFSFIEKVHLEA**CEQVS
GLSHLCSFT*QKKNIYTKIIKTT*QKKVQNSD*KANKQQVKKQCHAPFSR*YAL*A*LFCR*LVANSCKLTY
IRGKFRK*SNKKANHLLT*FLLTEARNWTTTTNV
ENIPDQRLNE*ILSQLLLKLY*PKF*X

Figure 2

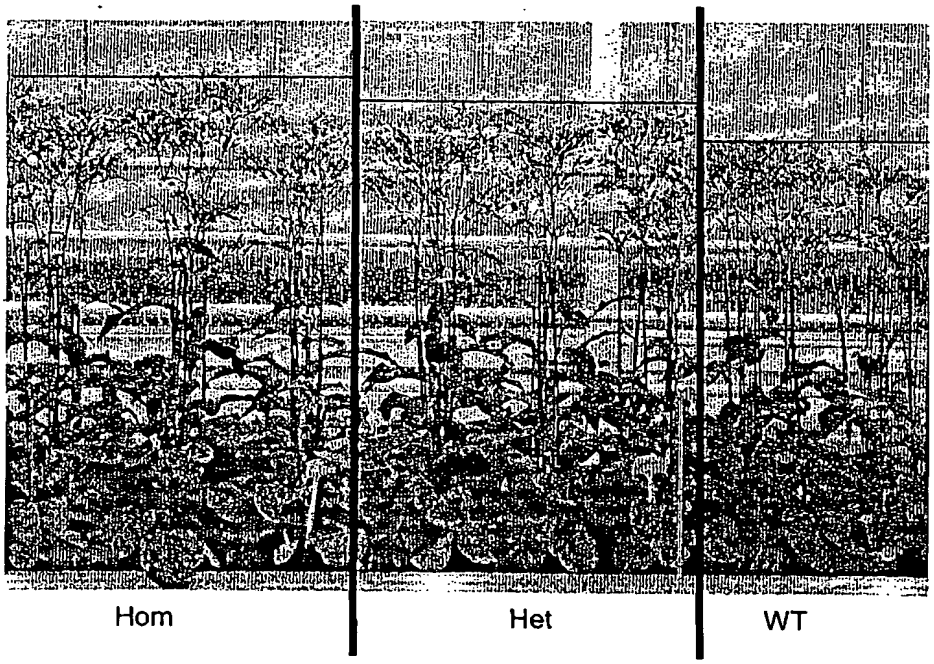
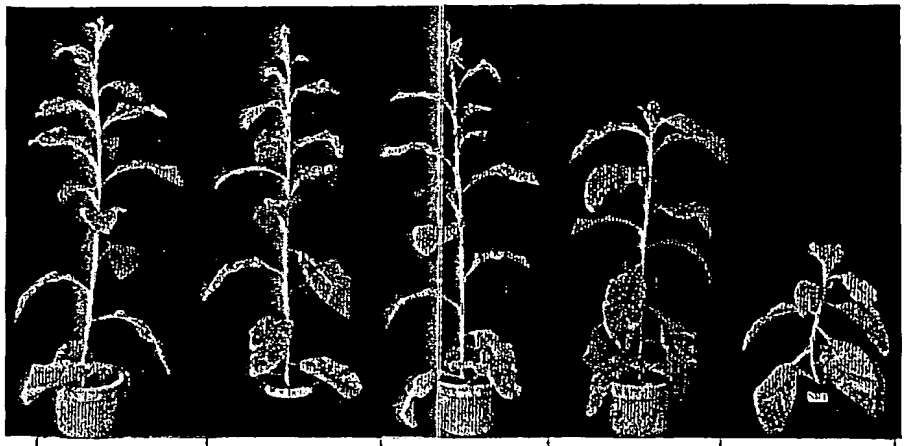


Figure 3



Plant ID	1	2	3	4	5
Transgenic (TG)	TG	TG	TG	TG	control
No of leaves	19	18	18	17	12/13

Figure 4

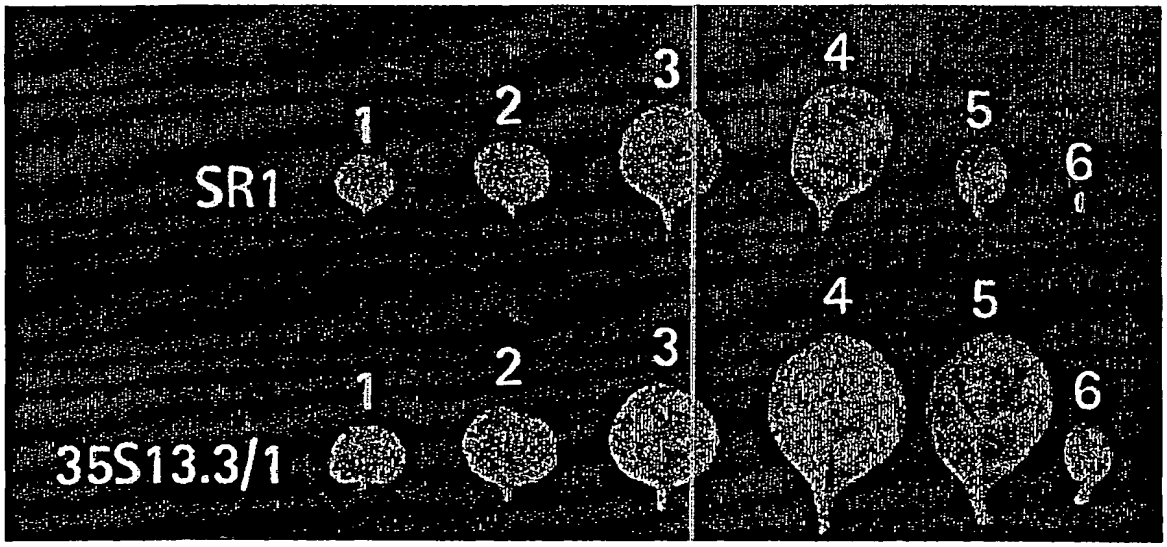


Figure 5